Evaluate Vantage

May 07, 2021

Arimoclomol failure leaves Biogen/Ionis exposed

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Biogen is under increasing pressure – as if it needs it – to deliver with its Ionis-partnered mRNA project tofersen in amyotrophic lateral sclerosis. The asset looks increasingly exposed among pivotal-stage ALS projects after the recent failure of Brainstorm's NurOwn and that of Orphazyme's arimoclomol, announced this morning. Investors will have to wait another week to find out the data from arimoclomol's pivotal ALS trial, Orarials-01, when these are presented at the Encals meeting; for now, Orphazyme says in the 245-patient study arimoclomol failed to beat placebo on either its primary measure, 76-week CAFS score, or secondary endpoints, which included the ALSFRS-R score and slow vital capacity. This comes after US FDA said Brainstorm's unequivocally negative pivotal study of the stem cell therapy NurOwn was insufficient for filing, Orion's levosimendan failed in the Refals trial, and Amylyx was told that it had to run a full phase 3 study with AMX0035. Tofersen's phase 3 Valor study, ending mid-2021, is the next big readout for ALS. In addition to failing in ALS arimoclomol has also flunked trials in inclusion body myositis and Niemann-Pick disease, though Orphazyme is pursuing a filing in the last indication.

Late-stage ALS pipeline (selected projects, excluding riluzole formulations)				
Project	**Mechanism**	**Company**	**Trial**	**Note**
Phase III				
Simdax po (levosimendan)	PDE3 inhibitor	Orion	NCT03505021 (Refals)	Failed Jul 2020
NurOwn Program One	Cell therapy	Brainstorm Cell Therapeutics	NCT03280056	Failed Nov 2020; data insufficient for filing
Arimoclomol citrate	SOD1 chaperone	Orphazyme (ex Cytrx)	NCT03491462 (Orarials-01)	Failed May 2021
Tofersen	SOD1 inhibitor mRNA	Biogen/Ionis	NCT02623699 (Valor)	183 subjects; data due H2 2021
Ultomiris	Anti-complement factor C5 Mab	Alexion	NCT04248465	382 subjects, ends Feb 2022
Alsitek (masitinib)	CD117, FGFR3 & PDGFR antagonist	AB Science	NCT03127267	495 subjects, not yet recruiting, ends Dec 2022
Phase II/III				
AMX0035 (sodium phenylbutyrate + Taurursodiol)	Histone deacetylase inhibitor + bax inhibitor	Amylyx	NCT03127514 (Centaur)	Centaur met primary endpoint, but FDA has demanded a full ph3 trial
CuATSM	Unknown	Collaborative Medicinal Development	NCT04082832	80 subjects; study ended, no data
Zilucoplan	Complement factor C5 inhibitor	UCB	NCT04436497 (HEALEY ALS Platform Trial – Regimen A)	160 subjects, ends Oct (previously Mar) 2021
Verdiperstat	Myeloperoxidase enzyme inhibitor	Biohaven	NCT04436510 (HEALEY ALS Platform Trial – Regimen B)	161 subjects, ends Oct (previously Mar) 2021
CNM-Au8	Elemental gold nanocrystals	Clene Nanomedicine	NCT04414345 (HEALEY ALS Platform Trial – Regimen C)	162 subjects, ends Oct (previously Mar) 2021
Ketas (ibudilast/MN-166)	LTD4 receptor antagonist	Medicinova	NCT04057898 (Combat-ALS)	230 subjects, ends Dec 2023
Source: clinicaltrials & Evaluate Pharma.				